

REMARKS

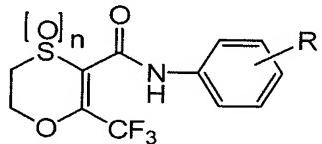
The Advisory Action dated March 23, 2009, indicates that Applicants' request for reconsideration in their Amendment dated March 4, 2009, but that the application was not in condition for allowance because of the absence of an error analysis for the data presented by Applicants. As discussed below, Applicants maintain that structural differences and their data together are sufficient to support the allowability of their claims.

Rejection under 35 U.S.C. 103

Claims 19-22, 28, and 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the Korean language paper by Hahn et al, *Han'guk Nonghwa Kakhoechi* (translated as *J. Korean Soc. Agric. Chem. Biotechnol.*), 44 (3), 191-196 (2001). Applicants note that the English translation of the Hahn et al paper that was kindly provided by the Examiner refers to antibacterial activity, whereas the English abstract attached to the original paper refers to antifungal activity. Based on context, Applicants will use the terms "fungicide" or "fungicidal" when referring to or citing the Hahn et al paper. Applicants respectfully traverse.

The Advisory Office challenges the sufficiency of the data presented in several Declarations under 37 C.F.R. 1.132 because of the absence of an error analysis of the data. Applicants, however, maintain that both the structural differences between their claimed compounds and the compounds disclosed in the reference and the dramatically enhanced fungicidal activity of their inventive compounds are more than sufficient to overcome any inference of obviousness.

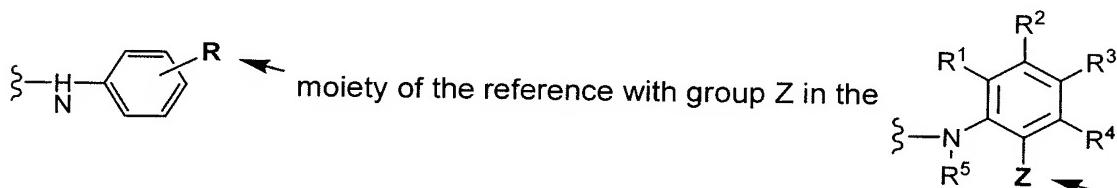
First, Applicants maintain that structural features distinguish their claimed compounds from the compounds of the reference. As has been fully discussed in Applicants' previous Amendments, the Hahn et al paper in Table 1 discloses a limited number and variety of dihydro-1,4-oxathiin carboxanilides of the formula



in which **n** is 0, 1, or 2 and **R** is hydrogen or one or two narrowly defined substituents that include methyl, trifluoromethyl, ethyl, isopropyl, methoxy, isopropoxy, methylthio, fluoro, chloro, bromo, nitro, and cyano. The reference in Table 2 also provides test data for some of these compounds. Based on the considerably better results for

compounds 21 (where R is 3-isopropoxy) and 40 (where R is 3-isopropyl) and on the known excellent fungicidal activity of "flutoranil" (more generally known as flutolanil, which also has a meta-isopropoxy phenyl moiety), the authors concluded that "the isopropoxy group or isopropyl group at the meta location of its phenyl group plays an important role" in fungicidal activity of such compounds. See translation at pages 15-16 (emphasis added). In view of the stated preference for meta-substitution of the benzene ring with isopropoxy or isopropyl groups, Applicants submit that the Hahn et al paper would not lead those skilled in the art to other types of groups located at an ortho position, a specified requirement for the Y group of Applicants' invention.

Although Applicants believe this level of analysis should be sufficient to distinguish their claimed invention from the teachings of the Hahn et al paper, a closer examination of the respective chemical structures is even more indicative of their differences. As pointed out in Applicants' most recent previous Amendment, one can readily see these differences by comparing group R in the

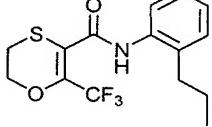
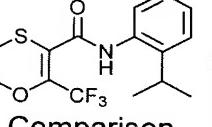
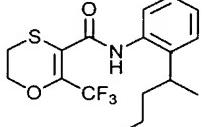


moiety of Applicants' claimed compounds. It may be noted that group R of the Hahn et al paper is only optional since R can be hydrogen. Even when present, group R is limited to relatively simple groups such as alkyl (including the preferred isopropyl group), alkoxy (including the preferred isopropoxy group), halogen, and the like. The Hahn et al paper cannot be read as teaching or even suggesting embodiments of Applicants' claimed invention in which group Z – the only phenyl substituent required by Applicants – represents Z² (i.e., cycloalkyl or bicycloalkyl groups) or Z⁴ (i.e., substituted C₂-C₂₀-alkenyl or C₂-C₂₀-alkynyl groups or combined with R⁴ to form a carbocyclic or heterocyclic ring). Even for compounds of Applicants' invention in which Z is Z³, the Hahn et al paper does not disclose or suggest compounds in which its group R could be an unsubstituted alkyl group having at least five carbon atoms or a substituted alkyl group of any length that must have a chlorine or cycloalkyl substituent as specified by Applicants for group Z³.

Applicants therefore again submit that these structural features are sufficiently different that those skilled in the art would not be led to their claimed invention.

Second, Applicants submit that the data they presented in the previously presented Declarations of Dr. Ulrike Wachendorff-Neumann and Dr. Arnd Voerste fully support the patentability of their claimed invention. The Final Office Action at page 3 (as reiterated in the Advisory Action) questions the reliability of the data because “[f]irst and foremost, there is no error analysis provided.” However, as observed by the Court of Customs and Patent Appeals in *In re Kollmann and Irwin*, 595 F.2d 48, 201 U.S.P.Q. 193, 199 (footnote 8) (C.C.P.A. 1979), a case in which the statistical significance of test data was also at issue, there is “no reason to question the data on this basis without some indication either from the data or the prior art that these types of tests give unreliable results.” The Final Office Action at pages 3-4 asserts in this regard that Applicants’ data are unreliable because the *Sphaerotilus* tests reported in two of the Declarations produced different results for comparison compound 53 of the Hahn et al paper, thereby “suggest[ing] a statistical problem in the measurements.” Applicants, however, have fully explained the single perceived anomaly in the test results and again refer to the established principal that “when an applicant demonstrates substantially improved results . . . and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary.” *In re Soni*, 54 F.3d 746, 751, 34 U.S.P.Q.2d 1684, 1688 (Fed. Cir. 1995) (emphasis added). For reasons that will again be explained below, Applicants submit that the Final Office Action and the Advisory Action have not only been overly zealous in discounting the *Sphaerotilus* test data but have also improperly ignored the strong data from the other tests.

For the convenience of the Examiner in considering their arguments, Applicants again summarize the test results in the following table, which shows the structures of the tested compounds, the organisms and application rates used in the tests, and the observed test results. By way of reminder, Applicants note that each comparison compound is characterized by a phenyl ring having a three-carbon alkyl substituent (one of which is linear and the other of which is branched) and each inventive compound is characterized by a phenyl ring having a five-carbon alkyl substituent (each of which is branched but not at the same carbon atom).

Test	Efficacy (%)			
				
<i>Sphaerotheca</i> (cucumber) 100 ppm (W-N D1) ⁽²⁾	—	10	—	98
<i>Venturia</i> (apple) 100 ppm (W-N D1) ⁽²⁾	—	57	—	100
<i>Uromyces</i> (bean) 100 ppm (W-N D2) ⁽³⁾	—	10	95	—
<i>Alternaria</i> (tomato) 500 ppm (Voerste) ⁽⁴⁾	0	0	95	—
<i>Sphaerotheca</i> (cucumber) 500 ppm (Voerste) ⁽⁴⁾	0	0	94	—

⁽¹⁾ Comparison compound (similar to but not identical to Hahn et al)

⁽²⁾ W-N D1 – From first Wachendorff-Neumann Declaration

⁽³⁾ W-N D2 – From second Wachendorff-Neumann Declaration

⁽⁴⁾ Voerste – From Voerste Declaration

Applicants first address the asserted deficiencies in the *Sphaerotheca* test data, which they assume is based on the slightly greater activity observed for comparison compound 53 at 100 ppm as reported in the first Wachendorff-Neumann Declaration than observed for the same compound at 500 ppm as reported in the Voerste Declaration. It should again be noted that because the experiments were not carried out under identical conditions (e.g., the solvents were different) or even on the same day, some variation in test results is not surprising. However, even if one were to assume – solely for the sake of discussion – that the results from this test could vary by as much as 10% (or 20% or even 30%), the differences in efficacies for comparison compound 53 and inventive compounds 39 and 102 are so great that

those skilled in the art would still conclude that the inventive compounds exhibit surprisingly and unexpectedly enhanced efficacies in this test compared to the comparison compound. Moreover, the *Sphaerotheca* test was not the only test used. The Final Office Action provides no objective evidence that the other tests are not valid or reliable.

Furthermore, the Board of Patent Appeals and Interferences, in a case where the so-called Colby formula had been applied to statistically thin data, observed that statistical significance is mostly an issue “where the differences in question are fairly small.” *Ex parte Quadranti*, 25 U.S.P.Q.2d 1071, 1073 (B.P.A.I. 1992) (emphasis added). Here, in contrast, the differences in the test data are not small but are instead quite robust, meaning that the presence or absence of a statistical analysis should not be a dispositive factor. Applicants again point out that four different tests were carried out against four different organisms using two different application rates. In every single test, Applicants’ inventive compounds always exhibited very high efficacy, whereas the comparison compounds did not. Even in the *Venturia* test, which gave the “closest” results, the differences in efficacy are dramatic. That is, regardless of the organism and the application rate and despite only modest structural differences for each tested pair of compounds, Applicants’ inventive compounds always exhibited dramatically greater efficacies than the respective comparison compounds. In view of these consistently greater efficacies, Applicants submit that even without a strict statistical analysis, those skilled in the art would conclude that the compounds of their claimed invention are patentably distinct from the compounds taught by the Hahn et al paper.

Applicants therefore again respectfully submit that their claimed invention is not rendered obvious by the Hahn et al paper.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

By Richard E. Henderson
Richard E. L. Henderson
Attorney for Applicants
Reg. No. 31,619

Bayer CropScience LP
2 T.W. Alexander Drive
Research Triangle Park, NC 27709
Ph.: (919) 549-2183
Fax: (919) 549-3994

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